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EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
10/05/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/567,979	Al-LAMEE ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,22 and 23* is/are pending in the application.

4a) Of the above claim(s) *10-20 and 22-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 4, 2009 has been entered.

Election/Restrictions

To summarize the current election, applicant elected Group I and the species where Formula I is poly(vinylbutyral-co-vinylalcohol-co-vinylacetate) with a Mw from 50,000 to 80,000, and 88% vinylbutyral groups and Formula II is poly(vinylpyrrolidone-co-vinylacetate) with an average Mw of 50,000. (It is noted that the restriction requirement did not require specification of the polymers' molecular weights)

Claims 10-20 and 22 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Upon further review, the restriction of claim 22, drawn to a vehicle from the coating composition under examination is hereby withdrawn because a search of this invention did not present an undue burden.

Newly submitted claim 23 is directed to an invention that lacks unity with the invention originally claimed for the following reasons: the common technical feature (a composition comprised of a bioactive, a polymer of a vinyl acetate and optionally a vinyl acetal and a vinyl alcohol, as well as a polymer of vinyl pyrrolidone and optionally vinyl acetate) in the inventions was previously shown in the prior art based upon the teachings of Ding in view of Eder. As the rejections below detail, Whitbourne et al. also suggest this composition in their teachings of a coating composition with the claimed terpolymer and poly(vinyl pyrrolidone) as preferred polymer components along with a bioactive agent (see below for further detail and citation).

Since applicants have received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 23 is withdrawn from consideration as being directed to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ding (previously cited) in view of Hsu et al. (previously cited) and the Technical Information on Kollidon VA 64 reference (previously cited; henceforth the Kollidon VA 64 reference) as evidenced by Li et al. (US PGPub No. 2002/0026234).

Ding teaches a drug-containing poly(acetal) based coating for an implantable medical device, where stents are exemplified as envisioned devices (see abstract and column 5 lines 22-30). In particular, Ding teaches a terpolymer of vinyl butyral, vinyl

alcohol and vinyl acetate (first compound) as the poly(acetal) in the coating composition (see claim 2, column 3 lines 21-27; instant claims 1 and 5). Variants of this polymer have the vinyl butyral constituting about 88% of the polymer backbone, with about 11% vinyl alcohol and the balance vinyl acetate (see column 3 lines 52-54; instant claims 6 and 7). The molecular weight (M_w) of this polymer is taught to be between 40,000 and 250,000 (see column 3 lines 31-32; instant claim 7). "In the case where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed.Cir. 1990)" (see MPEP 2144.05). Here the taught molecular weight range contains the claimed range of 50,000 to 80,000; therefore this claimed range is obvious in light of the range taught by Ding (see instant claim 7). Ding goes on to teach particularly envisioned drugs to include within the coating composition and these include both rapamycin and dexamethasone, as well as compounds that inhibit restenosis (see claims 2-3, column 5 lines 51-55, and column 6 lines 26-27 and 32; instant claim 8). An example demonstrates that Ding et al. contemplated the drug (bioactive material) to be present in the coating at about 1:2 drug to polymer (vehicle) (see example 5; instant claim 9). Further, Ding teaches that the poly(acetal) may be blended with other polymers where hyaluronic acid, a known lubricious agent, and vinyl acetate, are taught (see claim 10, column 4 lines 48-51, and column 5 lines 1-2 and 14 as well as Li et al. paragraph 8; instant claims 1 and 22). Ding does not specifically teach a copolymer of vinyl pyrrolidone and vinyl acetate as the "other" polymer.

Hsu et al. teach a coating composition for implantable medical devices that confers lubricity to the device surface (see abstract and column 1 lines 10-11). Hsu et al. go on to suggest the inclusion of a polyvinylpyrrolidone-vinyl acetate copolymer (second compound) in the coating to enhance the lubricity to the coating (see column 3 lines 56-60 and column 9 lines 31-35; instant claim 1). A lubricity enhancing compound is exemplified in the coating composition at 0.4% and 0.5%, including solvent, or 43% and 49%, without solvent (see table 1 one step solution and example 3 solution B; instant claim 2).

The Kollidon VA 64 reference teaches a polyvinylpyrrolidone-vinyl acetate copolymer known for use in drug delivery and film forming applications (see page 1 section 1.1, page 7 section 3.1, and page 8 section 3.3). The polymer is taught to have 60% vinylpyrrolidone and 40% vinyl acetate (see page 4 section 1.2; instant claim 3). Further, the molecular weight (M_w) it taught to be between 45,000 and 70,000 (see page 6 section 2.10). The teaching of 45,000 is interpreted as equivalent to the claimed "about 50,000" (see instant claim 4).

Since the implantation of a stent would be facilitated by it having a lubricious outer surface (e.g. easier and faster implantation) and Ding contemplates lubricious polymers as "other" polymers in their coating composition, it would have been obvious to one of ordinary skill in the art at the time the invention was made to select a polyvinylpyrrolidone-vinyl acetate copolymer as a particular "other polymer" to use in the invention of Ding and employ it at the taught percentages (use of known technique to similar product to improve in the same way). In particular, the selection of the

polyvinylpyrrolidone-vinyl acetate known as Kollidon VA 64 would have been an obvious choice for this artisan because it was available at the time of the invention, known for use in drug delivery and films, and the selection would be the simple substitution of one known element for another with a predictable outcome. Thus it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a polyvinylpyrrolidone-vinyl acetate copolymer with a 60:40 ratio of vinylpyrrolidone to vinyl acetate and a molecular weight of about 50,000 in the drug containing coating of Ding in view of Hsu et al. (see instant claim 22). Applicants do not teach any additional structure or components in the a coating in order for it to be "configured to release bioactive material" when the device on which it is coated is implanted; therefore the coating of Ding in view of Hsu et al. and the Kollidon VA 64 reference as evidence by Li et al. which contain the claimed first compound, second compound and bioactive material, meets this limitation. Thus claims 1-9 and 22 are obvious over Ding in view of Hsu et al. and the Kollidon VA 64 reference as evidence by Li et al.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ding in view of Hsu et al. and the Technical Information on Kollidon VA 64 reference as evidence by Li et al. as applied to claims 1-9 and 22 above, and further in view of Sass (previously cited).

Ding in view of Hsu et al. and the Technical Information on Kollidon VA 64 reference as evidence by Li et al. make obvious a coating composition with poly(vinylburtyral-co-vinylalcohol-co-vinylacetate) with a M_w from about 50,000 to

80,000, and 88% vinylbutyral groups, poly(vinylpyrrolidone-co-vinylacetate) (PVP/VA) with an average M_w of about 50,000, and a bioactive agent that inhibits restenosis. This modified reference does not explicitly teach the inclusion of 17β-estradiol.

Sass teaches that 17β-estradiol is known to inhibit smooth muscle cell growth and is used to inhibit restenosis and in-stent stenosis (see column 2 lines 50-57; instant claim 8).

Since Ding teaches the inclusion of compounds that inhibit restenosis in the coating composition, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ 17β-estradiol in the coating composition of Ding in view of Hsu et al. and the Technical Information on Kollidon VA 64 reference as evidenced by Li et al. as the simple substitution of one known element for another with a predictable outcome. Therefore claims 1-9 are obvious over Ding in view of Hsu et al., the Technical Information on Kollidon VA 64 reference, and Sass as evidence by Li et al.

Claims 1, 5-6, 9, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitbourne et al. (US Patent No. 6,110,483) as evidenced by Dupont et al. (US Patent No. 5,026,771) and Dhaliwal et al. (Thermochimica Acta 2002 391:245-255).

Whitbourne et al. teach a coating for implantable medical devices that is composed of both polymers and a bioactive agent (see abstract). Specifically the coating is envisioned to contain a bioactive agent, stabilizing polymer, and hydrophilic

polymer (see column 3 lines 50-52). The hydrophilic polymer is preferably PVP or PVP/VA (second compound) and the stabilizing polymer is preferably polyvinylbutyral (first compound), where BUTVAR® B-79 is an envisioned variety (see column 3 lines 21-26, 32, and 43-44 and column 5 line 66-column 6 line 1 and 25-26; instant claims 1 and 22). Dupont et al. teach that BUTVAR® B-79 is composed of 87 wt% vinyl butyral, 12 wt% vinyl alcohol and 1 wt% vinyl acetate (see column 7 lines 53-58; instant claims 5-6). Dhaliwal et al. teach that polyvinylbutyral is a random terpolymer of vinyl butyral, vinyl alcohol and vinyl acetate (see page 245 column 2 paragraph 2-246 column 1 line 9; instant claim 1). Example 19 of Whitbourne et al. teaches a ratio of 2:9 bioactive agent to total stabilizing polymer and hydrophilic polymer (see instant claims 9).

Although Whitbourne et al. do not provide an example that combines their envisioned polyvinylbutyral and PVP/VA with a bioactive agent, it would have been obvious to one of ordinary skill in the art at the time of the invention to follow their teachings and combine the preferred stabilizing polymer and hydrophilic polymer along with a bioactive agent to prepare their coating for its touted flexibility and adhesion to the device substrate. It additionally would have been obvious to follow the suggestion of their example and include the bioactive agent at a ratio of 2:9 relative to the total stabilizing polymer and hydrophilic polymer. Applicants do not teach any additional structure or components in the a coating in order for it to be "configured to release bioactive material" when the device on which it is coated is implanted; therefore the coating of Whitbourne et al. as evidenced by Dupont et al. and Dhaliwal et al. which contain the claimed first compound, second compound and bioactive material, meets

this limitation since this ratio was explicitly taught for the bioactive agent containing coating. Therefore claims 1, 5-6, 9, and 22 are obvious over Whitbourne et al. as evidenced by Dupont et al. and Dhaliwal et al.

Response to Arguments

Applicants' arguments, filed December 4, 2009, have been fully considered but they are not deemed to be persuasive.

Regarding the rejection under 35 USC 103(a) over Ding in view of Hsu et al.:

Applicants argue that the addition of lubricity enhancing components to the coating of Ding is fatally flawed because there would be no benefit had by increasing the lubricity of a stent coating. Applicants further contend that the presence of such components would be a disadvantage for a stent. These are attorney arguments that are not supported by evidence on the record. The state of the art at the time of the invention concerning lubricious coatings and agents on stents is demonstrated by Anderson et al. (US Patent No. 6,254,634), Hosteller et al. (US Patent No. 5,849,368), Zhong et al. (US PGPub No. 2003/0003220) ,and Tartaglia et al. (US PGPub No. 5,700,286). Both Anderson et al. and Hostettler et al. explicitly teach the application of lubricious coatings on stents (see Anderson et al. column 12 lines 22-25; Hostettler et al. column 7 lines 15-21). Tartaglia et al. go a bit further and also teach that a lubricious surface on stents protects the stent from the guide (used for insertion) or body lumen into which it is inserted by providing low surface friction (see column 3 lines 3-8). Zhong

et al. teach lubricious coatings on stents to reduce the stress exerted on the stent during deployment (see paragraph 27). Therefore, lubricious coatings were not only contemplated in general on stents but were utilized for particular reasons which include protection of the stent and reduction of friction during deployment (protection of stent and lumen). While applicants' suggestion that excessive lubricity would be detrimental to the ultimate function of a stent is a valid concern for stent surfaces, the artisan of ordinary skill would also have had this concern and sought to balance the desire for lubricity to protect the stent and ease deployment with the need for the stent to remain in place once positioned. Applicants' highlighting of the passage in the Kollidon VA 64 reference discussing the strong hydrophilicity of PVP/VA ultimately supports the contention that one of ordinary skill would have been aware of the properties associated with this class of polymers and would have sought to balance the benefits of its lubricity with the negatives of this same property that could occur when it is too intense (due to high concentration) or in a non-ideal locale (inner surface of stent). Similarly, the concern for the retention of a stent on the deployment catheter would also be a concern for the artisan of ordinary skill practicing the invention of Ding such that they would be able to apply their skills in the art and locate the coating on the outer surface of the stent, as suggested by the rejection, or tailor the amount of this component such that stent slippage from the deployment catheter would not be an issue.

Applicants also argue that the teachings of Hsu et al. do not suggest that PVP/VA is a lubricious polymer. Applicants dispute the interpretation of sections of Hsu et al. that were highlighted in the rejections and cite an additional section in the

reference to support their position. Both column 3 lines 55-60 and column 9 lines 31-35 were cited in support of the interpretation that PVP/VA was considered as a lubricious polymer by Hsu et al. These sections are shown below:

Column 3 lines 55-60:

> Another variation of the present invention discloses coating compositions wherein the biocompatible agent is a hydrophilic polymer. In various embodiments, the hydrophilic polymer is selected from the group consisting of polyvinylpyrrolidone (PVP), PVP/vinyl acetate copolymer, and polyethylene oxide.

Column 9 lines 31-35:

> The coating compositions of the present invention may further comprise a hydrophilic molecule or compound which enhances the lubricity of the coating. Suitable hydrophilic compounds include, but are not limited to, PVP and copolymers of PVP.

Applicants further cite column 5 lines 49-56 (shown below) to support their contention that lubricious properties in the coating of Hsu et al. are not due to the presence of PVP/VA and that this component would be expected to inhibit or ruin the lubricity of the coating of Hsu et al.

Column 5 lines 44-56:

> of the present invention. The stable, biocompatible coatings applied to the surfaces of devices (e.g. medical devices) are multi-functional in that they not only impart a high degree of lubricity to the surface of the device, but also provide a crosslinked network into which other biocompatible molecules may be affixed or entrapped. These additional functionalities can be imparted to the multi-functional bioactive surfaces of the present invention through the simple additional step of linking or entrapping biocompatible agents into the crosslinked polymer network forming the surface coating. Thus, these enhanced biocompatible or bioactive properties can be achieved without sacrificing the lubricating properties of the unmodified, crosslinked surface coatings. (It should be understood that "biocompatible" agents,

While the section from column 5 suggests that the presence of some biocompatible agents in the coating might be expected to interfere with the lubricious properties of the coating, it does not explicitly state that PVP/VA is such a biocompatible agent. In light of the explicit teachings by Hsu et al. that PVP and copolymers of PVP are hydrophilic compounds that enhance lubricity, that PVP and PVP/VA are hydrophilic polymers considered as biocompatible agents in the invention, and the fact that PVP/VA is the only PVP copolymer mentioned by name, it would have been reasonable for one of ordinary skill in the art to interpret this set of teachings as an indication that PVP/VA can serve as a lubricious coating component on medical devices. Applicants have provided no evidence that the presence of vinyl acetate in PVP/VA would have been expected to completely negate the explicitly taught lubricious properties of PVP and its copolymers. In addition, the interpretation of PVP/VA as known lubricious component for medical device coatings is consistent with the state of the art at the time of the invention. Clark et al. teaches both PVP and PVP/VA as preferred lubricious coating materials for a

medical device (see US PGPub No. 201000200542 paragraphs 14 and 20 and claims 1, 4, and 7). Applicants have not provided any evidence that PVP/VA would not have been expected to provide lubricity when included in a coating. The properties of adhesion (e.g., to a surface as an applied film) and rewettability highlighted in the submitted specification sheet for PVP/VA do not speak to any potential inability to function as a lubricious agent. Moreover, the highlighted teachings of Hsu et al. do not support the contention that PVP/VA was considered to provide properties detrimental to a lubricious coating. Therefore the interpretation of PVP/VA as a lubricious/lubricity enhancing component based upon the teachings of Hsu et al. was valid. This rejection has been slightly modified to include an evidentiary reference concerning the lubricious coating components taught by Ding.

Regarding the rejection under 35 USC 103(a) over Ding in view of Hsu et al. and Sass et al.:

Applicants argue that the teachings of Sass are irrelevant to the coatings described by Ding, Hsu et al. and the Kollidon VA 64 reference. Like Ding, Sass teaches a coating on a stent that contains an anti-restenotic compound as bioactive agent. For this reason, the teachings of Sass are relevant to those of Ding in view of Hsu et al. and the Kollidon VA 64 reference.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Juliet C Switzer/

Primary Examiner, Art Unit 1634